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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,257	04/14/2004	Lindsay H. Burns	14938US02	8108

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EXAMINER	
CLAYTOR, DEIRDRE RENEE	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/10/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

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Office Action Summary	Application No.	Applicant(s)	
	10/825,257	BURNS ET AL.	
	Examiner	Art Unit	
	Renee Claytor	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-54,72-74,77,80,83,87,96-103,106,111-127,130,133,141,143-151,153 and 158-173* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/20/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-54,72-74,77,80,83,87,96-103,106,111-127,130,133,141,143-151,153 and 158-173.

DETAILED ACTION

Applicant's election without traverse of Group I in the reply filed on 3/5/2007 is acknowledged. Applicant's election of the species of naltrexone, morphine, gabapentin, aspirin, ibuprofen, desipramine, ketamine, A-85380, bupivicaine hydrochloride and allodynia is also acknowledged. Claims 1-4, 6, 8-10, 14, 22-54,72-74, 77, 80, 83, 87, 96-103, 106, 111-127, 130, 133, 141, 143-151, 153 and 158-173 are being examined on their merits herein.

Claim Rejections – 35 U.S.C. – 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear as to what the amount of the antagonist is less than an effective antagonistic amount is referring to.

Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear what "the pharmaceutically acceptable carrier in the composition is a slow release agent" is referring to.

Claim 4 recites the limitation "the excitatory opioid receptor antagonist". There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6, 8-10, 14, 22-53, 72-74, 77, 80, 87, 96-103, 106, 111-127, 130, 133, 141, 143-151, 153 and 158-173 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of certain types of neuropathic pain such as allodynia and hyperalgesia, does not reasonably provide enablement for the treatment of all types of neuropathic pain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention: The rejected claims are drawn to a method of treating neuropathic pain comprising administration of an opioid antagonist.

(2) The state of the prior art: The state of the art regarding treating various types of neuropathic pain is relatively high. However the state of the art for the treatment of all types of neuropathic pain with all opioid antagonists is underdeveloped.

(3) The relative skill of those in the art: The relative skill of those in the art is high.

(4) The breadth of the claims: Claims embrace a method for treating neuropathic pain comprising administration of an opioid antagonist.

(5) The amount of guidance or direction presented: In the instant case, working examples are presented for treating hyperalgesia with the opioid antagonists alone and in combination with an agonist on pages 43-50 in the specification. Studies were performed in a rat model of two types of neuropathic pain, allodynia and hyperalgesia, in which naloxone or naltrexone and morphine were administered separately or in combination. As a result of the treatment, alleviation of allodynia with treatment of naltrexone and morphine occurred. However, there are a lack of working examples presented in the specification as filed showing how to treat all types of neuropathic pain with opioid antagonists. Note that lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP § 2164.

(7) The presence or absence of working examples: Applicant provides working examples for treating allodynia with opioid antagonists and agonists. However, applicant does not provide any working examples for treating all types of neuropathic pain with opioid antagonists and agonists.

(8) The quantitation of experimentation necessary: Claims read on a method for treating neuropathic pain comprising administration of an opioid receptor antagonist. As discussed above, the specification provides examples for treating allodynia, but the specification fails to provide sufficient support for treating all types of neuropathic pain with opioid compounds. Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections – 35 U.S.C. § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 rejected under 35 U.S.C. 102(b) as being anticipated by Levine (US Pg-Pub 2002/0016331).

Levine teaches a method of treating pain, including neuropathic pain, that comprises administering to a human a composition comprising an opioid antagonist (paragraph 0020 and 0029).

Claim Rejections – 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-4, 6, 8-10, 14, 22-45, 47-54, 72-74, 77, 80, 83, 87, 96-100, 102-103, 106, 111-127, 130, 133, 141, 143-147, 149-151, 153 and 158-173 rejected under 35 U.S.C. 103(a) as being unpatentable over Mitch et al. (U.S. Patent 5,998,434) in view of Romans et al. (7,015,371) and Sawynok et al. (6,211,171) and Frome (2003/0060463) and Fairbanks et al. (6,054,461) and Rueter et al. (2003/0216448) and Mayer et al. (5,502, 058).

Mitch et al. teach a method for treating pain in which it is taught that opioid antagonists and opioid agonist-antagonist combinations are useful (Col. 27, lines 54-57). Preferred opioid antagonists include naltrexone and a preferred agonist is morphine (Col. 27, lines 57-61). Mitch et al. further teach that non-steroidal anti-inflammatory drugs, including aspirin and ibuprofen, are also useful in the compositions of the invention (Col. 27, lines 23-29). It is taught that compositions of the invention are useful in the sciatic nerve ligation model, which is an animal model to treat allodynia (Col. 32, 15-35). The compositions of the invention include a colloidal dispersion system, a diluent, a binder, a plasticizer and preservatives (Col. 31, lines 40-64). The compositions can be administered orally, intravenously, intramuscularly, subcutaneously and transdermally (Col. 27, lines 14-19). The compound can be

administered to mammals and humans (Col. 31, lines 54-57). It is further taught that active compounds will be administered in a dose range of 0.005 to about 500 mg/kg of body weight (Col. 27, lines 2-3).

Mitch et al. do not teach a method of treating neuropathic pain in a patient with a composition comprising gabapentin, desipramine, ketamine, anti-dynorphin antibodies, A-85380, bupivicaine hydrochloride, intrathecal administration, or daily dosage regimens.

Romans et al teach a method of treating neurogenic pain, including mechanical allodynia (Col. 7, lines 3-6) using von Frey testing for pain behavior (Col. 7, lines 35-37). Morphine sulfate and gabapentin were tested for analgesia in mechanical allodynia and analgesia was observed after administration of morphine and gabapentin (Table 1).

Sawynok et al. teach a method of producing analgesia using tricyclic antidepressants, with desipramine being a preferred compound (Col. 9, lines 23-26, 66-67 and Col. 10, line 1). Desipramine was tested in the spinal nerve ligation model of neuropathic pain (Col. 12, lines 53-59).

Frome et al. teach a method of treating allodynia with ketamine (paragraph 0084, 0086 and 0090).

Fairbanks et al. teach that allodynia can be induced by dynorphin (Col. 3, lines 6-7); therefore it would be obvious that an anti-dynorphin antibody would be produced as an immune response to pain.

Rueter et al. teach a method for pain reduction (including allodynia; paragraph 0030, 0033). The NNR agonist A-85380 was used in a model of neuropathic pain (Example 3).

Mayer et al. teach the use of the compounds such as ketamine (Col. 3, line 39) and bupivicaine hydrochloride (Col. 6, lines 28-29) to treat neuropathic pain, which is defined as hyperalgesia or allodynia (Col. 1, lines 28-42).

Furthermore, it is obvious to vary and/or optimize the amount of naltrexone and morphine provided in the composition, according to the guidance provided by Mitch et al. and Roman et al., to provide a composition having the desired properties such as the desired concentrations of opioid antagonist and opioid agonist to effectively treat allodynia. It is also obvious to vary and/or optimize the dose of opioid antagonist that will enhance the potency of the opioid agonist. It is also obvious to vary and/or optimize the treatment regimen of administration of the opioid antagonist or opioid antagonist-agonist combination, according to the guidance provided by Mitch et al, to provide the most efficient treatment regiment to effectively treat allodynia. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Accordingly, it would have been obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of the prior art references because each reference individually teaches the various compounds for treating allodynia, a form of neuropathic pain. It is prima facie obvious to combine compositions each of which is

taught by the prior art to be useful for the same purpose (treatment of allodynia), in order to form a composition to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. In re Kerkhoven, 626 F.2d 846, 205 USPQ 1069, 1072 (CCPA 1980). Furthermore, one would be motivated to combine opioid antagonists with the various compounds listed in an effort to maximally treat allodynia.

Claims 43, 46, 98, 101, 145 and 148 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman & Gilman's: The Pharmacological Approach to Therapeutics (Tenth edition, page 8).

Goodman & Gilman's teaches various common routes of drug administration therefore making it obvious to utilize any route for drug administration of the present invention (pages 5-8).

Accordingly it would have been obvious to one having ordinary skill in the art at the time of the invention to administer the claimed composition by any known route of drug adminisration as is taught by Goodman & Gilman's. One would have been motivated to provide drug delivery any known form in order to achieve the most rapid effect of the drug.

Conclusion

No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Renee Claytor whose telephone number is 571-272-8394. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Renee Claytor

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER